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Enzymatic synthesis of the chiral neurotransmitter noradrenaline

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PURPOSE OF THE ABSTRACT

Green chemistry and biocatalysis has become a core field in the industrial biotechnology world, due to the need for sustainable and affordable methods for producing pharmaceuticals, fine chemicals and polymers, but most importantly due to enzymes' excellent catalytic efficiency.

The aim of our project is to identify target enzymes and structurally related homologues to be cloned, expressed, and used in biocatalytic assays against target compounds at Sterling Pharma Solutions. We will perform docking studies of chemical compounds within the enzyme models, and enzyme engineering to develop and enhance substrate specificity and overall yield. Enzyme immobilisation will be applied to enhance stability and performance. Finally, we aim to identify enzymes that are not commercially available from the open databases and produce them in-house, while lead candidate enzymes with great potential in biocatalysis and customer interest will be used in scale-up productions.

Currently, our focus is on the development of the ketoreductase (KRED) superfamily. It has been demonstrated that KREDs are incredibly selective in the reduction of a variety of ketones, including bridged ring systems and rings with five, six, and seven members. One very known function common to the KRED superfamily is the transformation of ketones to chiral alcohols. At Sterling, our initial efforts are to synthesise the chiral neurotransmitter noradrenaline (compound 3, fig. 1) which can be accessed from the chloroketone (1) after treatment with hexamine.

At the fundamental level, this project will offer the expertise and tools necessary to quickly produce customised enzyme solutions, made possible by the emerging fields of computational biochemistry and molecular biology, and will establish where biocatalysis can be offered as an alternative solution instead of the chemical synthesis. This is in line with Sterling's future to onboard biocatalysis and produce enzymes in-house, which will result in the development of a new core technology platform entitled Sterling Platform for Enzyme Engineering and Development (SPEED).

FIGURES

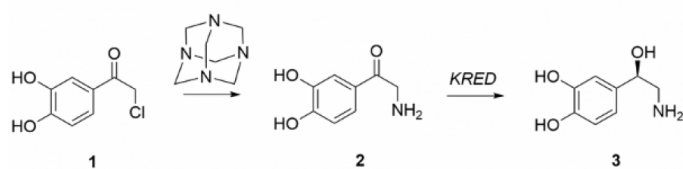


FIGURE 1

Fig. 1. Proposed route to noradrenaline, 3, from commercially available chloroacetone, 1.

Proposed route to noradrenaline, 3, from commercially available chloroacetone, 1.

FIGURE 2

KEYWORDS

enzymatic synthesis | biocatalysis | computational analysis and molecular docking | drug development

BIBLIOGRAPHY